Claims 19, 20, and 23 contain subject matter of claims 1, 2, and 11, respectively, revised to address the rejection of record, as explained below. Claims 21 and 22 contain subject matter of claim 9, claims 24, 25, 26, and 27 contain subject matter of claim 12, and claims 28 and 29 contain subject matter of claim 14, revised to address the rejections of record, as explained, below.

The present claims are limited to the examined subject matter, i.e., in accordance with the restriction and election of species requirements of record.

The objection to claim 4 and the rejections of record as applied against claims 3-8, 10, 13, and 15-18 are rendered moot by the cancellation hereby of claims 3-8, 10, 13, and 15-18.

Reconsideration is requested with respect to the rejections of record as applied against claims 1, 2, 9, 11, 12, and 14 under 35 USC 101, 35 USC 112, ¶1, 35 USC 112, ¶2, and 35 USC 102(e), in view of the changes to the claims effected, hereby, in conjunction with the following remarks.

By the changes to the claims effected, hereby, all the issues raised in the §101 rejection as applied against claims 1, 2, and 12, and in the §112, ¶2, rejection as applied against claims 9, 11, 12, and 14, are resolved. As such, withdrawal of the rejection is in order. Applicants wish to thank the Examiner for kindly suggesting changes in claim language that would overcome these rejections as applied against some of the claims at issue.

Reconsideration is requested with respect to the rejection under 35 USC 112, ¶1, for alleged lack of enablement, as applied against claims 1, 2, 9, 11, and 14. The present claims are limited to the subject matter in the rejected claims considered enabled in accordance with the statement of

rejection. As such, withdrawal of the rejection as applied against claims 1, 2, 9, 11, and 14, is, therefore, in order.

Reconsideration is requested with respect to the rejection under 35 USC 112, ¶1, as applied against claim 12.

Present claims 26 and 27 limit the subject matter of claim 12 to the subject matter of non-rejected claim 5, i.e., use of a medicament containing a purified peptide having the sequence ERRGHLRPSFHGHHEKGKEGQVLQRS (OB-CDGF) (SEQ ID NO: 10), i.e., "the medicament according to claim 21," and the purified peptide having a cell-proliferative effect on osteoblasts, i.e., "the medicament according to claim 23," respectively. Thus, the claims are limited to subject matter in claim 12 considered enabled in accordance with the statement of rejection. Withdrawal of the rejection as applied against claim 12, is, therefore, in order.

In connection with the rejection under §102(e), lack of novelty is alleged based on US5869638 (Takeshita). The subject of Takeshita is a protein OSF-4, which can be used as an agent for treating bone metabolic diseases, and of which the DNA can be used as a diagnostic agent. The allegation in the statement of rejection (Office Action, page 8) that the "sequence of Takeshita is 100% identical to the instant sequence," i.e., SEQ ID NO: 10, is not correct.

The protein OSF-4 comprises 796 amino acids, of which only amino acid residues 26 to 51 are identical with the sequence of OB-CDGF. A person skilled in the art in view of Takeshita is not able to arrive at the subject matter of the presently claimed invention. Takeshita does not include any hint or suggestion, which might lead to a peptide of the invention. For anticipation under § 102

to exist, each and every claim limitation, as arranged in the claim, must be found in a single prior art reference. *Jamesbury Corp. v. Litton Industrial Products, Inc.*, 225 USPQ 253 (Fed. Cir. 1985). The absence from a prior art reference of a single claim limitation negates anticipation. *Kolster Speedsteel A B v. Crucible Inc.*, 230 USPQ 81 (Fed. Cir. 1986). A reference that discloses "substantially the same invention" is not an anticipation. *Jamesbury Corp.* To anticipate the claim, each claim limitation must "*identically* appear" in the reference disclosure. *Gechter v. Davidson*, 43 USPQ2d 1030, 1032 (Fed. Cir. 1997) (*emphasis added*). To be novelty defeating, a reference must put the public in possession of the identical invention claimed. *In re Donahue*, 226 USPQ 619 (Fed. Cir. 1985).

The passage in Takeshita column 4, lines 42-46, relied on in the statement of rejection merely includes a broad teaching that fragments of OSF-4 of at least of 10 or 15 amino acids might be functional. Especially in view of the experimental data provided in Takeshita, this is merely speculation, at best, an invitation to experiment. A person skilled in the art has no incentive to prepare a fragment of OSF-4 of 26 amino acids residues. Even if the skilled artisan would wish to prepare such a fragment, he would face 770 different possibilities. Considering that actually he could prepare fragments of abut 10 to about 50 amino acids residues, the skilled artisan would face about 40000 options.

In other words, the person skilled in the art is aware that even such an unrealistic mass preparation of peptide fragments might eventually not be successful at all, because the disruption of

protein sequences usually leads to the loss of structure and activity, and many proteins are known to function only due to their three-dimensional structure.

Furthermore, Takeshita teaches away from generating an active peptide fragment from the -terminus of OSF-4. It was previously known and also reflected in Takeshita, that the functional domains of OSF-4 comprise the EC-domains 1-5, the TM-domain and the CP-domain (see figure 1 and table 4 in Takeshita). Amino acids 26 to 51 are located –terminal before those domains. According to the state of the art, the amino acids 26 to 51 were regarded as a presequence, which is cleaved during the processing of the cadherin, and after cleavage is a non-functional waste product. Therefore, a person skilled in the art in view of Takeshita, with the aim to create functional fragments would focus on the known or predicted active regions of the functional domains.

Therefore, the subject matter of the presently claimed invention, disclosing a specific peptide of 26 amino acids, and having a cell-proliferative effect on osteoblasts, is inventive over Takeshita et al.

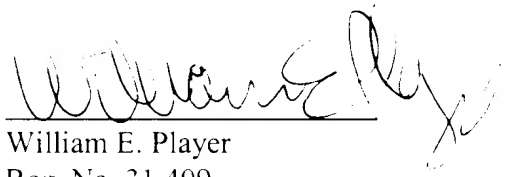
Furthermore, the rejection is at least questionable in view of the statements made in the Office Action concerning unity of invention. The Office Action (page 2) states: "Different sequences constitute different products because they constitute diverse coding regions and/or impart structural and functional differences." On page 5, the Office Action states: "It is known from . . . proteins, that even a single...amino acid change or mutation can destroy the function of the biomolecule in many cases." In the passage starting in the last paragraph on page 5, the Office Action considers the generation of fragments of variants as undue experimentation, which could not be required from a

skilled artisan. In summary, the Office Action relies on the allegation that a large protein does not inherently disclose a peptide and its activity, as stated on page 8, line 6.

Favorable action is requested.

Respectfully submitted,

JACOBSON·HOLMAN PLLC

By: 

William E. Player
Reg. No. 31,409

400 Seventh Street, N.W.
The Jenifer Building
Washington, D.C. 20004
Tel.: (202) 638-6666
Attorney Docket No. P65315US0
Date: February 10, 2003
WEP/rdt
R:\rthomas\2003\FEBRUARY\P65315US0-Amdt.wpd